Stanford

Livnat Jerby

Assistant Professor of Genetics

Bio

BIO

Livnat Jerby is an Assistant Professor in the Department of Genetics at Stanford University, a Chan Zuckerberg Biohub Investigator, and a Paul Allen Distinguished Investigator. Her research focuses on multicellular processes as a disease driver and therapeutic avenue, particularly in the context basic immune functions and properties. Using engineering-based, high-throughput approaches, she aims to gain insights into mechanisms and principles that govern immune responses and develop new "hybrid" platforms across in-vitro/in-vivo/in-silico systems that will allow us to identify tissue remodeling and immunomodulating interventions at an accelerated pace.

As a postdoctoral fellow in Aviv Regev's lab at the Broad Institute of MIT and Harvard, she studied T cell exclusion and dysfunction. Her work identified new mechanisms controlling cellular and tissue immunogenicity and demonstrated the potential of epigenetic reprogramming as a therapeutic modality to overcome immunotherapy resistance in cancer. Dr. Jerby holds a B.Sc. in Computer Science and Biology and obtained her PhD in 2016 from Tel Aviv University, where she worked with Prof. Eytan Ruppin, studying non-linear genetic interactions.

Dr. Jerby joined Stanford University in November 2020. Integrating genetic engineering, single-cell genomics, imaging, and machine learning, her laboratory develops high-throughput systems to study cellular circuits at greater scale, resolution, and depth, aiming to identify new and more diverse immunomodulating mechanisms and interventions and develop strategies to target and engineer endogenous and synthetic immune circuits, with potential implications for disease treatment and prevention.

Dr. Jerby’s research has been generously supported by the Schmidt Family Foundation, Rothschild Foundation, the Cancer Research Institute (CRI), the Burroughs Wellcome Fund (BWF), Ovarian Cancer Research Alliance (OCRA), Paul G. Allen Family Foundation, Bill and Melinda Gates Foundation, and Chan Zuckerberg Biohub initiative.

ACADEMIC APPOINTMENTS

- Assistant Professor, Genetics
- Member, Bio-X
- Member, Stanford Cancer Institute

HONORS AND AWARDS

- Allen Distinguished Investigator, Paul G. Allen Family Foundation (2022 - 2025)
- Liz Tilberis Early Career Award, Ovarian Cancer Research Alliance (2022 - 2025)
- Investigator award, Chan Zuckerberg biohub (2020 - 2025)

- Career Awards at the Scientific Interface (CASI), Burroughs Wellcome Fund (BWF) (2019 - 2024)
- Postdoctoral training fellowship, Cancer Research Institute (CRI) (2016-2019)
- Postdoctoral award, Eric and Wendy Schmidt Foundation (2016-2017)
- Postdoctoral fellowship, Rothschild, Yad Hanadiv (2015-2016)

PATENTS

- Aviv Regev, Pratiksha Thakore, John Doench, JT Neal, Jesse Boehm, Oana Ursu, Livnat Jerby-Arnon. "United States Patent 16/809,458 Methods and Compositions for Massively Parallel Variant and Small Molecule Phenotyping"
- Aviv Regev, Livnat Jerby-Arnon, Ana Anderson, Katherine Tooley, Vijay K. Kuchroo. "United States Patent 17/083,235 Pan-Cancer T Cell Exhaustion Genes"
- A. Regev, O. Rozenblatt-Rosen, B. Izar, and L. Jerby. "United States Patent PCT/US2018/054020 and PCT/US2018/025507 Methods and compositions for detecting and modulating an immunotherapy resistance gene signature in cancer"
- Livnat Jerby, A. Regev, L. Jerby, M. Suva, N. Riggi. "United States Patent PCT/US2020/022466 Detection means, Compositions and Methods for Modulating Synovial Sarcoma Cells"

LINKS

- Lab website: http://jerbylab.stanford.edu/

Research & Scholarship

CURRENT RESEARCH AND SCHOLARLY INTERESTS

Overview. We develop high-throughput, engineering-based approaches to: (1) dissect and target multicellular regulation at greater scale, resolution, and depth, focusing on the molecular mechanics that govern innate and adaptive immune responses in cancer, (2) broaden the spectrum of immunomodulating interventions to trigger targeted immune responses in more effective and targeted ways, including antigen-independent modalities, (3) modify cells and groups of cells to augment or create new "synthetic" (multi)cellular circuits – allowing us to probe the “inner-workings” of multicellular processes and potentially form a basis for new types of disease treatment and prevention strategies.

Current efforts. Bringing together advances in genetic engineering, machine learning, and single-cell/spatial genomics, we study the interplay between cancer cells and cytotoxic lymphocytes, namely, CD8 T cells and NK cells. These types of cells are a very convenient model system, as we can modify them ex vivo, and then study them in vivo. We develop new multidisciplinary methods to identify regulators of cellular and tissue immunogenicity, and uncover mechanisms controlling lymphocyte activation/ suppression, recruitment, and infiltration.

Specific projects currently include: developing a multimodal perturb-seq system to identify key regulators of cancer-T-cell and cancer-NK interactions; mapping cancer-immune dynamics across time and space using emerging single-cell and spatial profiling technologies; and hybrid CRISPR-ML systems to identify combinatorial genetic perturbations to induce cytotoxic lymphocyte recruitment, infiltration and effector functions in the tumor microenvironment.

Teaching

COURSES

2023-24

- Genomics: GENE 211 (Win)

2022-23

- Biology and Applications of CRISPR/Cas9: Genome Editing and Epigenome Modifications: BIOS 268, GENE 268 (Spr)
- Genomics: GENE 211 (Win)

2021-22

- Biology and Applications of CRISPR/Cas9: Genome Editing and Epigenome Modifications: BIOS 268, GENE 268 (Spr)
- Genomics: GENE 211 (Win)

2020-21

- Cancer Biology Journal Club: CBIO 280 (Spr)

STANFORD ADVISEES

Doctoral Dissertation Reader (AC)

Alvina Adimoelja, Peter Du, Matt Grieshop, Mingxin Gu, Kathryn Hanson, Jessica Kain, Ann Lin, Eric Sun, Catherine Zhang

Postdoctoral Faculty Sponsor

Yuxin Cai, Youngmin Kim, Chang Sun, Jeehyun Yoe, Dixian Zhu

Doctoral Dissertation Advisor (AC)

Karmen Aguirre, Reece Akana, Celeste Diaz, Kristen Frombach, Mike Tsai

GRADUATE AND FELLOWSHIP PROGRAM AFFILIATIONS

- Genetics (Phd Program)

Publications

PUBLICATIONS

- **DIALOGUE maps multicellular programs in tissue from single-cell or spatial transcriptomics data.** *Nature biotechnology*
  Jerby-Arnon, L., Regev, A.
  2022

- **Opposing immune and genetic mechanisms shape oncogenic programs in synovial sarcoma.** *Nature medicine*
  Jerby-Arnon, L. n., Neftel, C. n., Shore, M. E., Weisman, H. R., Mathewson, N. D., McBride, M. J., Haas, B. n., Izar, B. n., Volorio, A. n., Boulay, G. n., Cironi, L. n., Richman, A. R., Broye, et al
  2021

- **A Cancer Cell Program Promotes T Cell Exclusion and Resistance to Checkpoint Blockade.** *Cell*
  Jerby-Arnon, L., Shah, P., Cuoco, M. S., Rodman, C., Su, M. J., Melms, J. C., Leeson, R., Kanodia, A., Mei, S., Lin, J. R., Wang, S., Rabasha, B., Liu, et al
  2018; 175 (4): 984-997.e24

- **Predicting Cancer-Specific Vulnerability via Data-Driven Detection of Synthetic Lethality** *CELL*
  Jerby-Arnon, L., Pfetzer, N., Waldman, Y. Y., McGarry, L., James, D., Shanks, E., Seashore-Ludlow, B., Weinstock, A., Geiger, T., Clemons, P. A., Gottlieb, E., Ruppin, E.
  2014; 158 (5): 1199–1209

- **Author Correction: Massively parallel phenotyping of coding variants in cancer with Perturb-seq.** *Nature biotechnology*
  Ursu, O., Neal, J. T., Shea, E., Thakore, P. I., Jerby-Arnon, L., Nguyen, L., Dionne, D., Diaz, C., Bauman, J., Mosaad, M. M., Fagre, C., Lo, A., McSharry, et al
  2022

- **Inter-cellular CRISPR screens reveal regulators of cancer cell phagocytosis.** *Nature*
  Kamber, R. A., Nishiga, Y., Morton, B., Banuelos, A. M., Barkal, A. A., Vences-Catalan, F., Gu, M., Fernandez, D., Seoane, J. A., Yao, D., Liu, K., Lin, S., Spees, et al
  2021

- **Multimodal pooled Perturb-CITE-seq screens in patient models define mechanisms of cancer immune evasion** *NATURE GENETICS*
  Frangieh, C. J., Melms, J. C., Thakore, P. I., Geiger-Schuller, K. R., Ho, P., Luoma, A. M., Cleary, B., Jerby-Arnon, L., Malu, S., Cuoco, M. S., Zhao, M., Ager, C. R., Rogava, et al
  2021: 332–41

- **Serine biosynthesis is a metabolic vulnerability in IDH2-driven breast cancer progression.** *Cancer research*
  Barnabas, G. D., Sang Lee, J., Shami, T., Harel, M., Beck, L., Selitrennik, M., Jerby-Arnon, L., Erez, N., Ruppin, E., Geiger, T.

2021

- **Inhibitory CD161 receptor identified in glioma-infiltrating T cells by single-cell analysis.** *Cell*
  Mathewson, N. D., Ashenberg, O. n., Tirosh, I. n., Gritsch, S. n., Perez, E. M., Marx, S. n., Jerby-Arnon, L. n., Chanoch-Myers, R. n., Hara, T. n., Richman, A. R., Ito, Y. n., Pyrdol, J. n., Friedrich, et al
  2021

- **A Distinct Transcriptional Program in Human CAR T Cells Bearing the 4-1BB Signaling Domain Revealed by scRNA-Seq.** *Molecular therapy : the journal of the American Society of Gene Therapy*
  Boroughs, A. C., Larson, R. C., Marjanovic, N. D., Gosik, K., Castano, A. P., Porter, C. B., Lorrey, S. J., Ashenberg, O., Jerby, L., Hofree, M., Smith-Rosario, G., Morris, R., Gould, et al
  2020; 28 (12): 2577-2592

- **A single-cell landscape of high-grade serous ovarian cancer** *NATURE MEDICINE*
  Izar, B., Tirosh, I., Stover, E. H., Wakiro, I., Cuoco, M. S., Alter, I., Rodman, C., Leeson, R., Su, M., Shah, P., Iwanicki, M., Walker, S. R., Kanodia, et al
  2020; 26 (8): 1271-+

- **A single-cell and single-nucleus RNA-Seq toolbox for fresh and frozen human tumors** *NATURE MEDICINE*
  Slyper, M., Porter, C. M., Ashenberg, O., Waldman, J., Drokhlyansky, E., Wakiro, I., Smillie, C., Smith-Rosario, G., Wu, J., Dionne, D., Vigneau, S., Jane-Valbuena, J., Tickle, et al
  2020; 26 (5): 792-+

- **Integrative molecular and clinical modeling of clinical outcomes to PD1 blockade in patients with metastatic melanoma** *NATURE MEDICINE*
  Liu, D., Schilling, B., Liu, D., Sucker, A., Livingstone, E., Jerby-Amon, L., Zimmer, L., Gutzmer, R., Satzger, I., Loquai, C., Grabbe, S., Vokes, N., Margolis, et al
  2019; 25 (12): 1916-+

- **Genome-wide prediction of synthetic rescue mediators of resistance to targeted and immunotherapy** *MOLECULAR SYSTEMS BIOLOGY*
  Das Sahu, A., Lee, J. S., Wang, Z., Zhang, G., Iglesias-Bartolome, R., Tian, T., We, Z., Miao, B., Nair, N., Ponomarova, O., Friedman, A. A., Amzallag, A., Moll, et al
  2019; 15 (3): e8323

- **IL-33 Signaling Alters Regulatory T Cell Diversity in Support of Tumor Development.** *Cell reports*
  Li, A. n., Herbst, R. H., Canner, D. n., Schenkel, J. M., Smith, O. C., Kim, J. Y., Hillman, M. n., Bhutkar, A. n., Cuoco, M. S., Rappazzo, C. G., Rogers, P. n., Dang, C. n., Jerby-Arnon, et al
  2019; 29 (10): 2998–3008.e8

- **Harnessing synthetic lethality to predict the response to cancer treatment** *NATURE COMMUNICATIONS*
  Lee, J., Das, A., Jerby-Arnon, L., Arafeh, R., Auslander, N., Davidson, M., McGarry, L., James, D., Amzallag, A., Park, S., Cheng, K., Robinson, W., Atias, et al
  2018; 9: 2546

- **Perturb-Seq: Dissecting Molecular Circuits with Scalable Single-Cell RNA Profiling of Pooled Genetic Screens** *CELL*
  Dixit, A., Pamas, O., Li, B., Chen, J., Fulco, C. P., Jerby-Amon, L., Marjanovic, N. D., Dionne, D., Burks, T., Raychowdhury, R., Adamson, B., Norman, T. M., Lander, et al
  2016; 167 (7): 1853-+

- **Genome-scale study reveals reduced metabolic adaptability in patients with non-alcoholic fatty liver disease** *NATURE COMMUNICATIONS*
  Hyotylainen, T., Jerby, L., Petaja, E. M., Mattila, I., Jantti, S., Auvinen, P., Gastaldelli, A., Yki-Jarvinen, H., Ruppin, E., Oresic, M.
  2016; 7: 8994

- **Fumarate induces redox-dependent senescence by modifying glutathione metabolism** *NATURE COMMUNICATIONS*
  Zheng, L., Cardaci, S., Jerby, L., MacKenzie, E. D., Sciacovelli, M., Johnson, T., Gaude, E., King, A., Leach, J. G., Edrada-Ebel, R., Hedley, A., Morrice, N. A., Kalna, et al
  2015; 6: 6001

- **Moving ahead on harnessing synthetic lethality to fight cancer** *MOLECULAR & CELLULAR ONCOLOGY*
  Jerby-Arnon, L., Ruppin, E.
  2015; 2 (2): e977150

- **Metabolic Associations of Reduced Proliferation and Oxidative Stress in Advanced Breast Cancer** *CANCER RESEARCH*
  Jerby, L., Wolf, L., Denkert, C., Stein, G. Y., Hilvo, M., Oresic, M., Geiger, T., Ruppin, E.
  2012; 72 (22): 5712–20

- **Predicting Drug Targets and Biomarkers of Cancer via Genome-Scale Metabolic Modeling** *CLINICAL CANCER RESEARCH*
  Jerby, L., Ruppin, E.
  2012; 18 (20): 5572–84

- **Haem oxygenase is synthetically lethal with the tumour suppressor fumarate hydratase** *NATURE*
  Frezza, C., Zheng, L., Folger, O., Rajagopalan, K. N., MacKenzie, E. D., Jerby, L., Micaroni, M., Chaneton, B., Adam, J., Hedley, A., Kalna, G., Tomlinson, I. M., Pollard, et al
  2011; 477 (7363): 225–U132

- **Predicting selective drug targets in cancer through metabolic networks** *MOLECULAR SYSTEMS BIOLOGY*
  Folger, O., Jerby, L., Frezza, C., Gottlieb, E., Ruppin, E., Shlomi, T.
  2011; 7: 501

- **Computational reconstruction of tissue-specific metabolic models: application to human liver metabolism** *MOLECULAR SYSTEMS BIOLOGY*
  Jerby, L., Shlomi, T., Ruppin, E.
  2010; 6: 401